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DIABETIC NEPHROPATHY IN THE FAMILY PRACTICE SETTING: CLINICAL NOTE

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Diabetic nephropathy is a well known complication of both insulin-dependent and non-insulin dependent diabetes mellitus. The classic findings of diabetic nephropathy are albuminuria, hypertension, and progressive renal insufficiency. Primary care physicians can efficiently monitor for the end organ complications of diabetes at routine office visits. Urinary evaluation for microalbumin is an effective was to monitor for the effects of hyperglycemia on the kidneys.

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DIABETIC NEPHROPATHY IN THE FAMILY PRACTICE SETTING: CLINICAL NOTE

ABSTRACT:

Diabetic nephropathy is a well known complication of both insulin-dependent and non-insulin dependent diabetes mellitus. The classic findings of diabetic nephropathy are albuminuria, hypertension, and progressive renal insufficiency. Primary care physicians can efficiently monitor for the end organ complications of diabetes at routine office visits. Urinary evaluation for microalbumin is an effective was to monitor for the effects of hyperglycemia on the kidneys.

BACKGROUND:

Diabetic nephropathy is a well known syndrome of albuminuria, hypertension, and progressive renal insufficiency that was described by Kimmelsteil and Wilson in 1936. Diabetic nephropathy can progress to end-stage renal disease (ESRD), eventually leading to dialysis and to kidney transplantation.

In patients with insulin-dependent diabetes mellitus (IDDM) for 20 years, the incidence of ESRD is 40%. The incidence of ESRD in whites is lower among patients with non-insulin-dependent diabetes mellitus (NIDDM). Because there are many more people with NIDDM, the number of people with NIDDM who develop ESRD is approximately equal to the number of people with IDDM who develop ESRD. In black, hispanic, and native American populations there is a higher incidence of ESRD in NIDDM. Approximately one-third of the new cases of ESRD in the United States are associated with diabetes. [1]

The pathophysiology of IDDM has been well studied. On initial diagnosis of diabetes the histology of the kidney is normal. Within three years, changes typical of diabetic glomerulosclerosis appear. These include thickening of the glomerular basement membrane and mesangial expansion which together form nodular glomerular lesions. Because of the increased kidney size, there is an increase in renal blood flow and in the glomerular filtration rate. Mild microalbuminuria may be present if the blood sugars are not well controlled. Because of the increased kidney size and the hyperfiltration, the serum creatinine and the urea nitrogen concentrations are usually slightly reduced. This stage - microalbumin in the range of 15-140 mcg/dl - is called ***Incipient Nephropathy***. [2] At this stage the nephropathy is very responsive to treatment.

After 10-15 years of IDDM the first laboratory evidence of renal damage may appear. The presence of microalbuminuria (30-300 mg per 24 hr) is an indication of renal damage. In the IDDM patients with concomitant hypertension, the presence of microalbuminuria is greatly increased. The worsening renal function leads to worsening hypertension which leads to a vicious downward spiral of renal function and quality of life. Diabetic nephropathy is diagnosed clinically when the patient has had diabetes for more than five years, has evidence of diabetic retinopathy and develops significant albuminuria (>300 mg per 24 hr) without evidence of other causes of kidney disease. When these criteria are met, the diagnosis can be made clinically without performing a renal biopsy. If the diagnosis is in doubt, a renal biopsy should be performed to look for nodular sclerosis of the glomerulus.

When clinical diabetic nephropathy has been present for about four years, the serum creatinine rises to 2 mg/dl or greater. In three additional years, about one-half of the patients will develop ESRD. The pathophysiology of diabetic nephropathy is not as clear cut in NIDDM.

Microalbuminuria is associated with the development of diabetic nephropathy. However, the precise level of microalbuminuria that is predictive of this condition has yet to be determined. In some patients, albuminuria may be due to the presence of other renal disorders such as obstructive uropathy, hypertension or atherosclerosis. It may even reflect an age-related increase in urinary albumin excretion.

The current literature shows that a strict regimen of blood sugar control and blood pressure control will reduce the morbidity caused by the end stage organ damage of diabetes mellitus. Diabetes, in specific hyperglycemia, is very rarely fatal. With the exception of diabetic ketoacidosis, most of the mortality associated with hyperglycemia is from end organ complications. The end organ damage also results in a major source of morbidity and the majority of office visits by these patients.

METHODS:

This study looked at the diabetic population at the Colorado Springs Osteopathic Foundation and Family Medicine Center (FMC). The FMC is an ambulatory care clinic whose primary emphasis is on making medical care available to the medically indigent and low income families in the area. The FMC supports a family practice residency program. At the time of the study, there were three senior residents, five junior residents, and four preceptors. In the FMC practice records reflected 52 patients with the diagnosis of diabetes, 10 patients with IDDM and 42 patients with NIDDM. This was a retrospective study of these patients by chart review. The charts were reviewed twice during the study in November 1994 and June 1995. All of the diabetic patients, Type I (IDDM) and Type II (NIDDM), were included in this review. Review parameters included hypertension, retinopathy, hyperlipidemia, proteinuria, microalbuminuria, and hemoglobinA1C (HbA1C). In each case, the parameters were used to tabulate the effects of hyperglycemia and end organ damage. (Fig. 1)

RESULTS:

The results were revealing in that, as a clinic, the FMC seemed to be very efficient at evaluating for most of the areas of potential end organ damage. The area in which the FMC was less effective was in assessing diabetic nephropathy. FMC staff more effectively utilize office tests and procedures than outside laboratory tests. However, laboratory tests are critical in the management of these patients. As previously mentioned, the criteria for diabetic nephropathy are albuminuria, retinopathy, and hypertension. In the FMC practice, 3 of 52 patients, all NIDDM, fell into this category. Another ten patients met two of the three criteria. (Fig. 2)

MANAGEMENT STRATEGIES:

Assessment:

The first step in effective management is to develop a routine to evaluate these patients. Diabetics are very complicated. One end-organ system frequently will dominate the majority of the office visits. It is very easy to get involved in the patients' immediate complaints and not take the time to step back and manage the whole person. An initial history and physical exam is performed on all new diabetic patients. Thereafter, an annual diabetic exam should be performed. This should consist of a review of the patient's history and an in-depth physical exam and laboratory evaluation. For an example of this, refer to Figure 3. These results should all be rechecked if changes in condition warrat reevaluation. Fasting finger stick blood sugar checks may be done during visits on a random basis to monitor for acute changes. Increases may signify infection or worsening glycemic control.

Treatment:

The treatment plan is the most dynamic part of the care of the diabetic population. This should be individualized to meet the needs of ther specific patient while emphasizing some basic elements. All patients should receive education regarding meal planning, exercise, the differences between the types of diabetes, and treatment options. Patients also should be informed about end organ diseases which can be made worse by poor glucose control. Informed patients are then able to ask questions, gather information, and better participate in management of their disease. One of the central philosophies in management is moderation. Moderation applies not only to food and drink, but to all elements of lifestyle.

Initial treatment consists of glucose control. Much has been written on the topic and there are many different regimens for achieving good control. A good personal goal for the patient is to have as near euglycemic blood sugars as possible. Ideally, the blood sugar range should fall between 100 and 200 mg/dl with less than 140 mg/dl being optimal. HbA1C levels also should be maintained as near normal as possible. HbA1C levels less than 8 represent excellent control. Less than 10 is fair control. The Diabetes Control and Complication Trial (DCCT) released their results in 1994.[3,4] This study was completed over nine years on isulin-dependent (Type 1) diabetics. From this study the American Diabetes Association (ADA) has released a revised version of their standards of care for diabetic patients. While it is not within the scope of this paper to cover this topic in depth, the DCCT reference provides extensive background.

The second step is blood pressure control. Many of these patients will have significant blood pressure problems. A measurement of 140 mmHg systolic and 90mmHg diastolic is a recognized hypertension standard. If the blood pressure is greater than this on three separate trials, these patients are termed hypertensive and treated. However, a rise in blood pressure, even if values remain in the normal range, may be significant. [5] In most cases a significant rise in blood pressure is associated with an increase in protein excretion. As well, this increase in pressure will have an effect on the eyes, carotid vessels, and coronary vessels. If this rise occurs, treatment with an Angiotensin Converting Enzyme (ACE) inhibitor or calcium channel blocker should also be considered.

A third area to consider for treatment is when a patient exhibits a microalbuminuria of 15-140 mcg/dl. This stage is called *incipient nephropathy* and is very responsive to treatment. The medications shown to be effective are likewise the ACE inhibitors and calcium channel blockers. Both agents have been well studied and are proven effective. They work at the level of the kidney to improve glomerular filtration and reduce intraglomerular pressures. [6] Intraglomerular pressures rise long before blood pressure rises. This leads to thickening and sclerosis of the basement membrane and mesangial expansion. On gross pathological examination the classical findings of nodular glomerular lesions can be seen. Serum renal functions show a slightly lowered BUN and CR in the incipient phase. The BUN and CR then begin to increase gradually as the nephropathy progresses. The function 1/CR can be plotted on the Y axis versus time on the X axis.[7] This will show a linear decline in renal function (Fig. 5). With treatment, the 1/CR curve can be moved upward and to the right. Treatment improves the renal function and lengthens the time to end-stage renal disease.

When initiating a medication, it is best to start with a low dosage to ensure that the medication is being tolerated. After 1-2 weeks the dosage is progressed until the patient is stabilized on a moderate level. Some patients will show a mild drop in blood pressure, but most of the normotensive patients will not exhibit a noticeable change. A urinalysis for microalbumin, a serum BUN and CR, and a fasting glucose should be rechecked in 3-6 months.

The medication is increased, walking the thin line between benefit and side effects. With two different classes of medication and the availability of multiple agents within each class, side effects and adverse reactions can be decreased. This gives clinicians some prescriptive options for maximizing benefits.

CONCLUSIONS:

The management of diabetes is a difficult task. Often there are varied and multiple complaints that can trap the physician into acute care scenarios with these patients. This makes it necessary for the provider to have a well thought out treatment plan, a regularly scheduled visit schedule for the patient, and a specific agenda to complete for each visit.

At the Family Medicine Center, the physicians are now looking carefully for end-organ complications of diabetes. Diabetic nephropathy is a complication that can be positively addressed with proper monitoring and treatment. With use of the dip-stick test for microalbumin, these patients can be evaluated early for signs of incipient nephropathy. Beginning treatment in this early stage provides the greatest potential for managing this situation, altering the curve, and slowing the progression toward end-stage renal disease.

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Figure 1. Parameters reviewed to evaluate for the end-organ complications of diabetes

	IDDM		NIDDM	
Microalbuminuria				
# checked	2	20%	5	12%
# positive (of those checked)	1	50%	3	60%
Proteinuria				
# checked	8	80%	33	79%
# positive	0	0%	11	33%
Hypertension				
# checked	10	100%	42	100%
# positive	2	20%	23	55%
Retinopathy				
# checked	10	100%	42	100%
# positive	0	0%	9	21%
HbA1C				
# checked	9	90%	35	83%
# positive	8	89%	25	71%
Hyperlipidemia				
# checked	7	70%	39	93%
# positive	2	29%	14	36%

Figure 2. Family Medicine Center patients with criteria for diabetic nephropathy

Microalbuminuria/proteinuria, Retinopathy, Hypertension

IDDM	NIDDM
0	3

Retinopathy and Hypertension

IDDM	NIDDM
0	5

MIcroalbuminuria/Proteinuria and Retinopathy

IDDM	NIDDM
0	1

Microalbuminuria/Proteinuria and Hypertension

IDDM	NIDDM
0	4

Figure 3. Sample annual diabetic exam form

Name_____ Date_____
Height_____ Weight_____ BP_____ Temp_____ Pulse_____ Resp_____
History CAD_____ HTN_____ Visual Changes_____ Last eye exam_____
Smoking_____pack/day/year ETOH_____#/day /month /year Numbness in feet____

Physical
Heent Ears infection hearing
Eyes Fundi AV Nicking Vessels Retinopathy
Nose/Throat
Neck Bruits Adenopathy Thyroid
Lungs Wheeze Rales Rhonchi
Heart Rhythm Rate Murmurs Size
Abd Obese Organomegally Bruits
Ext Cyanosis Clubbing Edema Sensation: vibratory positional
Foot Exam: Lesions Nails amputations
Gyn/Prostate

Laboratory
UA: Glucose___ Protein___ Leukocyte Esterase___ Bacteria___ Nitrite___
Creatinine_____ Microalbumin_____
CBC: WBC, Hb, HCT, Platelet, differential

SMA: Na, Cl, K, CO_2, Bun, Cr, Glucose, Mg, Ca, Liver profile, HbA1C

Baseline TSH T_4 T_3 T_7
EKG
Creatinine Clearance

Assessment
Diabetes IDDM NIDDM Retinopathy Nephropathy Neuropathy
Hypertension CAD

Plan
Individualized for each patient

Figure 4. End-organ systems worsened by poor glycemic control

Eyes: Retinopathy, Retinal Detachments, Blindness
Vascular: Coronary Artery Disease, Hypertension, Congestive Heart Failure, Atherosclerosis, Myocardial Infarction
Neurologic: Strokes, Neuropathies
Extremities: Amputations
Renal: Nephropathy, dialysis, transplant
Gastrointestinal: Gastritis, Gastroparesis
General: Increased incidence of infections

Figure 5. 1/CR may be plotted versus time to predict end-stage renal disease. This curve is moved to the right with treatment.

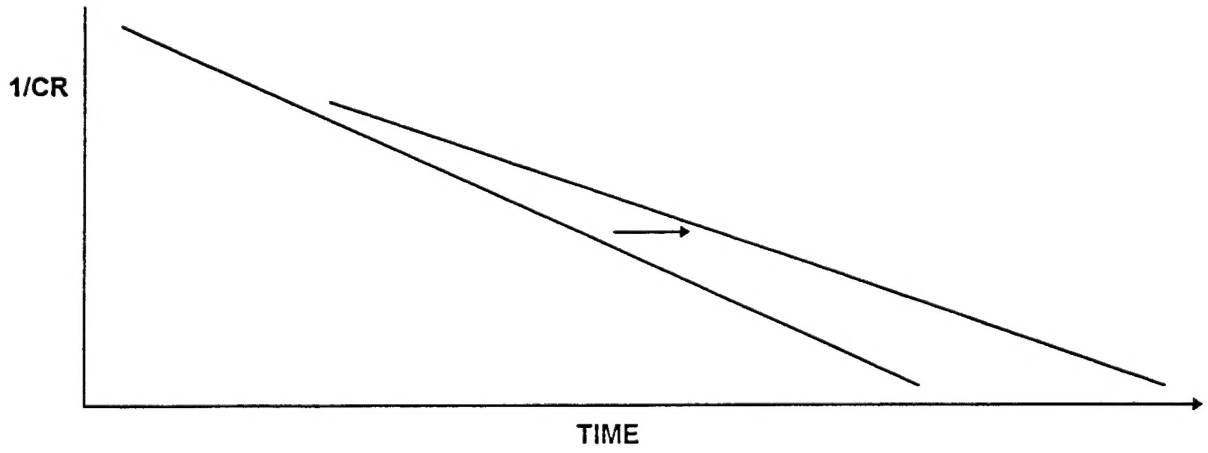

Figure 6. Age-related changes in creatinine and creatinine clearance

Age	Normal Serum CR (mg/dl)	Average CR Clearance (ml/min per 1.73 m2)
20-29	0.99 ± 0.16	110
30-39	1.14 ± 0.22	97
40-49	1.10 ± 0.20	88
50-59	1.16 ± 0.17	81
60-69	1.15 ± 0.14	72
70-79	1.03 ± 0.22	64
80-89	1.06 ± 0.25	47
90-99	1.20 ± 0.16	34

Figure 7. ACE inhibitors & calcium channel blockers

ACE Inhibitors	Calcium Channel Blockers
benzepril	amlodipine
captopril	bepridil
enalapril	diltiazem
fosinopril	felodipine
lisinopril	isradipine
quinapril	nicardipine
ramipril	mimodipine
	verapamil